RED CELL DISORDERS 🩸

Disorders of red blood cells (RBCs) primarily present as anemia, and less commonly as polycythemia (erythrocytosis).

ANEMIA – DEFINITION & CORE CONCEPT 📉

Anemia is defined as a decrease in red cell mass below normal, leading to a reduced oxygen-carrying capacity of blood.

🔑 Key point for exams:
Anemia is not defined by hemoglobin alone but reflects reduced red cell mass → ↓ tissue oxygenation.

I) PATHOGENETIC CLASSIFICATION OF ANEMIA (Basic mechanisms of anemia)

Anemia develops due to one or more of the following mechanisms:

1. Blood loss
2. Increased red cell destruction (hemolysis)
3. Decreased red cell production

📌 *Note:* In many disorders, more than one mechanism operates simultaneously

➡️ *Example:* Thalassemia = ↓ RBC production + ↑ RBC destruction

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ERYTHROPOIETIN RESPONSE IN ANEMIA 🩸

In most anemias (except chronic renal failure & chronic inflammation):

↓ Tissue oxygen tension → Renal peritubular interstitial cells sense hypoxia → ↑ Erythropoietin (EPO) production → Stimulation of erythroid precursors in bone marrow → Erythroid hyperplasia → ↑ RBC production

In severe anemia:

Bone marrow capacity exceeded → Extramedullary hematopoiesis → Liver, spleen, lymph nodes enlarge

📌 Exam pearl:
Chronic renal failure → ↓ EPO production → inadequate marrow response

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MARROW RESPONSE & RETICULOCYTE COUNT 🔬

Reticulocytes = newly formed immature RBCs

Hemolysis / Acute blood loss:

- ↑ RBC destruction or loss → Intact marrow response → ↑ Reticulocyte count (reticulocytosis)

Decreased RBC production (Aregenerative anemia):

- Bone marrow failure or ineffective erythropoiesis → ↓ Reticulocyte count (reticulocytopenia)

📌 Reticulocyte count is the single most useful test to differentiate:

- Hemolytic anemia vs
- Production failure anemia

II) MORPHOLOGICAL CLASSIFICATION OF ANEMIA 🔍

Anemia can also be classified based on RBC morphology, which gives strong etiologic clues.

Morphologic parameters assessed:

- Size
- Color (hemoglobin content)
- Shape

These are evaluated by:

- Peripheral blood smear (subjective)
- Automated red cell indices (objective)

RED CELL INDICES 📊

Index	Definition	Significance
MCV	Mean Cell Volume (fL)	Classifies anemia as microcytic, normocytic, macrocytic
MCH	Mean Corpuscular Hemoglobin (pg)	Average Hb per RBC
MCHC	Mean Corpuscular Hb Concentration (g/dL)	Hb concentration in packed RBCs
RDW	Red Cell Distribution Width	Measures variation in RBC size (anisocytosis)

📌 Exam tip:

↑ RDW suggests mixed populations of RBCs (e.g., iron deficiency)

IMPORTANT LABORATORY TESTS IN ANEMIA 🧪

1️⃣ Iron Studies

Used in microcytic anemias to differentiate:

- Iron deficiency
- Anemia of chronic disease
- Thalassemia

Includes:

- Serum iron
- TIBC
- Transferrin saturation
- Ferritin

2️⃣ Hemolysis Markers

Abnormal in hemolytic anemia:

- ↑ Unconjugated bilirubin
- ↓ Haptoglobin

- ↑ Lactate dehydrogenase (LDH)

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3 Vitamin Levels

Low in megaloblastic anemia:

- Serum & RBC folate
- Vitamin B12

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4 Hemoglobin Electrophoresis

Detects:

- Hemoglobinopathies
- Thalassemias
- Structurally abnormal hemoglobins

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5 Coombs Test

Detects:

- Antibodies or complement bound to RBCs → Used in immune-mediated hemolytic anemia

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WHEN IS BONE MARROW EXAM REQUIRED? 🦴

i) Isolated anemia:

➡️ Peripheral blood tests usually sufficient

ii) Anemia + cytopenias:

- Thrombocytopenia
- Granulocytopenia

➡️ Suggests:

- Marrow aplasia
- Marrow infiltration

➡️ Bone marrow examination warranted

CLINICAL CONSEQUENCES OF ANEMIA 🫀🫁

Depend on:

1. Severity
2. Rapidity of onset
3. Underlying cause

Slow-onset anemia – compensatory mechanisms:

↓ Oxygen delivery → ↑ Cardiac output → ↑ Respiratory rate → ↑ 2,3-DPG in RBCs → Enhanced O_2 unloading from hemoglobin

📌 These compensations:

- Effective in healthy individuals
- Ineffective in cardiac/pulmonary disease

Common Clinical Features:

- Pallor
- Fatigue
- Lassitude

III) CLASSIFICATION OF ANEMIA BY MECHANISM

1 Blood Loss

- Acute: trauma
- Chronic:
  - GI tract lesions
  - Gynecologic disorders

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2 Increased Destruction (Hemolytic Anemias)

A. Intrinsic (Intracorpuscular) Defects

Hereditary (MEH)

Membrane abnormalities

- Cytoskeletal:
  - Hereditary spherocytosis
  - Hereditary elliptocytosis
- Lipid defects:

- Abetalipoproteinemia

Enzyme deficiencies

- Hexose monophosphate shunt:
  - G6PD deficiency
  - Glutathione synthetase deficiency
- Glycolysis:
  - Pyruvate kinase deficiency
  - Hexokinase deficiency

Hemoglobin disorders

- Structural abnormalities:
  - Sickle cell anemia
  - Unstable hemoglobins
- Decreased globin synthesis:
  - Thalassemia syndromes

Acquired

- Paroxysmal nocturnal hemoglobinuria

B. Extrinsic (Extracorpuscular) Defects

Antibody-mediated

- Isohemagglutinins:
  - Transfusion reactions
  - Rh disease of newborn
- Autoantibodies:
  - Idiopathic
  - Drug-induced
  - Autoimmune diseases (e.g., SLE)

Mechanical destruction

- Microangiopathic hemolytic anemia:
  - TTP
  - DIC
- Prosthetic / dysfunctional cardiac valves

Infections

- Malaria

3 Impaired Red Cell Production (SEE - HIM)

Stem cell disorders

- Aplastic anemia
- Pure red cell aplasia

Erythroblast maturation defects

- Defective DNA synthesis
    - Vitamin B12 deficiency
    - Folate deficiency (megaloblastic anemia)

Erythropoietin deficiency

- Chronic renal failure

Iron dysregulation

- Anemia of chronic disease

Hemoglobin synthesis defects

- ↓ Heme synthesis:
    - Iron deficiency anemia
    - Sideroblastic anemia

- ↓ Globin synthesis:
    - Thalassemias

Marrow replacement / infiltration

- Acute leukemia
- Myelodysplastic syndromes
- Metastatic tumors
- Granulomatous disease → Myelophthisic anemia

-> The End <-